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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,530	05/09/2001	Kurt Klimpel	15280-290110	7146

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/853,530	KLIMPEL ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 31* is/are rejected.

7)☒ Claim(s) *30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Claims 1-6,30,31 are under consideration.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-6,31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Leppla et al. (WO 94/18332) in view of Noteborn et al. (WO 95/03414) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Leppla et al. teach anthrax protective antigen (see last paragraph page 25 and first paragraph, page 26) and a fusion protein containing the PA binding domain of LF/toxin, wherein toxins are commonly full length proteins(see last paragraph page 25 and second paragraph, page 26). Leppla et al. teach that the fusion protein can contain the first 1-254 amino acids of LF (e.g. PA binding domain)(see pages 6 and 7). The name anthrax as used by Leppla et al. refers to Bacillus anthracis (see last paragraph page 3, continued on next page). Processed protective antigen is created when the anthrax protective antigen is administered in vivo. Leppla et al. teach that the toxin/fusion protein and PA are administered as a pharmaceutical composition (see page 27) containing saline (aqueous solution of physiologically compatible salts, see page 28). Leppla et al. do not teach the conjugate contains a viral protein. Noteborn et al. teach

the intracellular viral protein VP3 which can be used to kill tumor cells and other target cells (see page 8, third paragraph and page 2, last paragraph). Noteborn et al. teach immunoconjugates containing VP3 and a ligand that can be internalized by a cell (see page 9, third paragraph). The PA/PA binding domain of LF/toxin conjugate is internalized by a cell(see Leppla et al., page 4, last paragraph, continued on page 5). Leppla et al. teach the use of the aforementioned two component system to deliver a molecule into a cell (see claim 19 and 20). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Leppla teach the claimed invention except for use of a viral protein whilst Noteborn et al. teach immunoconjugates containing the viral toxin VP3 and a ligand that can be internalized by a cell and Leppla et al. teach the use of the aforementioned two component system to deliver a molecule into a cell. The recitation of an intended use in this product claim carries no patentable weight because the claimed product is the same as the product rendered obvious in the instant rejection. The dosage recited in the claims (as per defined in page 20, penultimate paragraph of the specification) is encompassed by the dose range disclosed in page 27, lines 24-25 of Leppla et al. While Leppla et al. do not teach the molar ratio recited in claim 31, Leppla et al. teach that the amount of PA and LF/fusion protein will be optimized using routine procedures. One of ordinary skill in the art would have been motivated to do the aforementioned because Leppla et al. teach the use of the aforementioned two component system to deliver a molecule into a cell and Noteborn et al. teach immunoconjugates containing VP3 and a ligand that can be internalized by a cell.

Regarding applicants comments and the Leppla declaration, the recitation of an intended use carries no patentable weight in the instant product claims. In addition, the product rendered obvious in the instant rejection would have the same properties as the claimed invention because it is structurally identical to the claimed product. It is also noted that the motivation for producing the claimed product can be different from applicants as long as the same product is produced (see MPEP 2144).
Regarding the size of the toxin molecule used in the fusion protein, Leppla et al. teach anthrax protective antigen (see last paragraph page 25 and first paragraph, page 26) and a fusion protein containing the PA binding domain of LF/toxin, wherein toxins are

commonly full length proteins(see last paragraph page 25 and second paragraph, page 26). Leppla et al., page 26, second paragraph teaches uses of a toxin in the aforementioned fusion protein wherein toxin refers to a full length toxin. Said paragraph also refers to other full length proteins such as growth factors. Regarding applicants comments about Noteborn et al. said reference is cited for the use of VP3 viral toxin in the claimed conjugate. One of ordinary skill in the art would have been motivated to do the aforementioned because Leppla et al. teach the use of the aforementioned two component system to deliver a molecule into a cell and Noteborn et al. teach immunoconjugates containing VP3 and a ligand that can be internalized by a cell. Regarding applicants comments about paragraph 10 of the Leppla declaration, as per above, the motivation to produce the claimed invention cited in the instant rejection need not be the same as applicants as long as it leads to a product which is structurally the same as the claimed product. Furthermore, in KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

Regarding paragraph 11 of the Leppla declaration, the instant fusion protein would have the functional properties recited in claim 1 because the product is the same as the claimed invention. Whether the product rendered obvious in the instant rejection would also eventually kill the cell or generate a Class II mediated antibody response is irrelevant, because there is currently no limitation in the claims which prohibits either of the aforementioned activities. There is no evidence that the product rendered obvious in the instant rejection would not induce a MHC class I mediated CTL response. In fact, according to the Leppla declaration, it should induce a class I response because it would be targeted to the appropriate anatomic compartment for processing. Furthermore, it appears that paragraph 11 of the Leppla declaration indicates that the conjugate would be unable to kill cells because the toxic protein moiety would be processed. However, this is clearly inaccurate because both native APABP and the conjugates disclosed in Leppla et al. are cytotoxic. Furthermore, the VP3 protein disclosed by Noteborn et al. is both immunogenic and cytotoxic. The instant rejection

discloses why it is obvious to create a product that is structurally identical to the claimed invention.

Regarding applicants comments about "processed PA", the rejection refers to the processed PA of claim 2 (A.K.A. cleaved PA which reveals the LF binding site).

Regarding applicants comments that Leppla et al. do not disclose use of a viral protein in their conjugate, this issue is addressed by the addition of the Noteborn et al. (WO 95/03414) reference. Regarding applicants comments about dosage, the specification discloses on page 20 that:

> For each recipient, the total vaccine amount necessary can be deduced from protocols for immunization with other vaccines. The exact amount of such antigen- APABP and PA compositions required will vary from subject to subject, depending on the species, age, weight and general condition of the subject, the particular fusion protein used, its mode of administration, and the like. Generally, dosage will approximate that which is typical for the administration of other vaccines, and will preferably be in the range of about 10 ng/kg to 1 mg/kg.

Thus, regarding the functional dosage recited in the claims, said dosage will vary according to the antigen and particular parameters as per stated above. Said passage also discloses a general range of antigen to be used. Leppla et al., disclose administration of the instant invention at a dosage that overlaps that encompassed by the limitation now recited in the claims (see page 27, lines 24-25).

The recitation of an intended use carries no patentable weight in the instant product claims. In addition, because it is structurally identical to the claimed product, it would have the same properties as the claimed product. Furthermore, the claimed composition as disclosed in Leppla et al. could induce a CTL response depending on the recipient and the protein used. For example, virtually any protein would be immunogenic/induce CTL if administered into another species (e.g. the art recognizes that mouse Ig is immunogenic when administered to humans, etc). The invention rendered obvious in the instant rejection has the same structure as the claimed invention and would therefore have the same properties as the claimed invention. Regarding applicants comments that the viral protein recited in the claims would not kill the target, there is no limitation in the claims that the protein is not toxic to the cell. The CAV proteins disclosed by Noteborn are both cytotoxic and immunogenic (see claim 1). One of ordinary skill in the art would have been motivated to do the aforementioned because

Leppla et al. teach the use of the aforementioned two component system to deliver a molecule into a cell and Noteborn et al. teach immunoconjugates containing VP3 and a ligand that can be internalized by a cell.
Regarding applicants comments, the Leppla declaration has been fully considered and addressed.

4. The rejection of claims 1-6,30,31 under 35 U.S.C. 103(a) as being unpatentable over Milne et al. (Mol. Microbiology 15:651, 1995), Arora et al. (J. Biol. Chemistry 268:3334, 1993) or Leppla et al. US Patent 5,591,631 in view of EP 0 532 090A2 (issued March 3, 1991) and Donnelly et al . (PNAS 90:3530:1993) for the reasons elaborated in the previous Office Action is withdrawn in view of the Berzofsky declaration filed 2/17/06.

5. Claim 30 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron, Ph.D./
Primary Examiner, Art Unit 1644